



**UNITED STATES DEPARTMENT OF COMMERCE**  
**Patent and Trademark Office**

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EXAMINER

WITZ, J

ART UNIT

PAPER NUMBER

1808

DATE MAILED:

11/10/97

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

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## **DETAILED ACTION**

### ***Response to Arguments***

1. Applicant's arguments filed July 23, 1997 have been fully considered but they are not persuasive for the reasons set forth below.

### ***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

3. Claims 1-21 are rejected under 35 U.S.C. § 103 as being unpatentable over Lee et al. combined with Guidicelli et al. for the reasons of record.

Claims 1-19 are drawn to the reduction of adipose tissue at selected sites in the body comprising the introduction of collagenase and another proteinase into said tissue. Claim 20 is drawn to a method of reducing adipose tissue for cosmetic purposes. Claim 21 requires that the adipose tissue is reduced by at least 25%.

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Applicants assert that their invention “provides what can be called ‘chemical liposuction’” in that “the amount of adipose tissue at selected locations in the body is reduced for cosmetic purposes by introducing into said adipose tissue collagenase, or collagenase plus another proteinase.” Applicants further continue to argue that Lee does not disclose the in vivo administration of collagenase for the digestion of adipose tissue. Applicants allege that “there is nothing whatsoever in Lee et al. to make obvious or predictable that their enzymes could be used to digest the connective tissue of adipose tissue in vivo or what would happen to released fat.” Applicants further allege that “the body itself removes released fat from the selected location of the treatment, resulting in less fatty material there.”

Applicants’ characterization of both the claim language and the Lee et al. reference is much too narrow. The claim language recites that to reduce adipose tissue at a selected site in the body one administers to that adipose tissue collagenase or collagenase in conjunction with other proteinases so that the adipose tissue at the site is reduced. This method may be practiced for cosmetic purposes. This is all that is required of the claimed method.

In the analysis of the claim language, it is noted that Applicants claim the administration of collagenase to adipose tissue, which is defined as a type of connective tissue which is areolar connective tissue in which the nutrient-storing function is greatly increased. The storage cells are called adipocytes and are the main component of the tissue mass. The adipocytes contain pure neutral fat in the form of oil which occupies most of the cell’s volume. Very little matrix is

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present in adipose tissue and the tissue is richly vascularized due to the need to deliver fat to and from the storage tissue.

Lee et al. teaches that collagenase plus chymopapain digests connective tissue. Adipose tissue is particularly disclosed as being effectively digested so as to obtain endothelial cells present therein. Guidicelli et al. discloses that is conventional to use collagenase and trypsin for the purpose of digesting and isolating adipocytes. This teaching indicates that the collagenase is effective in hydrolyzing the matrix which holds the cells together. Further, it is expected that in the resulting hydrolysis of the matrix that fat cells will be damaged and disrupted, thereby releasing the oil within. There is clearly no effect of the collagenase on the fat contained in the adipocyte.

In further analysis of the claim language, it is noted that the claims only require that the amount of adipose tissue be reduced. The term "tissue" is defined as "an aggregation of morphologically and functionally similar cells" and "cellular matter regarded as a collective entity." As a result of disaggregation of these cells by dissolution of the connective tissue matrix, the tissue has been digested and therefore its amount has been reduced. If the adipocytes are in the least not in the form and function of a tissue, i.e. a group of closely associated cells that are similar in structure and perform a common function, no adipose tissue exists. As stated above, it is clear from the disclosure of Lee and Guidicelli that the effects of collagenase on adipose tissue result in the disruption of the tissue into cells and cell debris and therefore, whether in vitro or in vivo, collagenase reduces the amount of adipose tissue to which it has been applied.

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Further, the term “for cosmetic purposes” fails to define the claims over the prior art. These cosmetic purposes include such a wide range of applications such as treatment of fatty cysts such that one of ordinary skill in the art would be motivated as disclosed and taught in the patent to digest the connective tissue, i.e. adipose tissue, contained therein with a reasonable expectation of success of said digestion, thereby reducing the adipose tissue at said site.

Finally, Applicants’ characterization of the process as “chemical liposuction” is immaterial to the rejection at hand because such is not claimed. As stated previously, all that is required is that, at the time of the administration of the collagenase, the adipose tissue is disrupted and thereby reduced. One skilled in the art would reasonably expect that the administration of collagenase to adipose tissue would result in the digestion of the tissue, therefore effecting its reduction. As for the claims, what happens to the intact and ruptured adipocytes after the administration is immaterial to the claimed invention. Insofar as Applicants characterize the procedure as “chemical liposuction” and make comparisons of safety, such comparisons are not persuasive as the two procedures are in no way comparable in form or effect. As noted in the name, “liposuction” means the removal of fat from the body. With regards to the claimed invention, no fat has been removed from the body.

In view of the prior art, one of ordinary skill in the art would expect that, should he/she wish to reduce the amount of any connective tissue, including adipose tissue, at a site in the body, one would be motivated to use a composition well known to digest said tissue with a reasonable expectation of success. It is noted that absolute predictability is not required under the standard

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of obviousness of 35 USC 103; all that is required is a reasonable expectation of success. In re Long, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Optimization of dose is well within the skill of the practitioner as the enzyme kinetics of collagenase and other enzymes based upon amount of substrate are well known.

#### ***Conclusion***

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

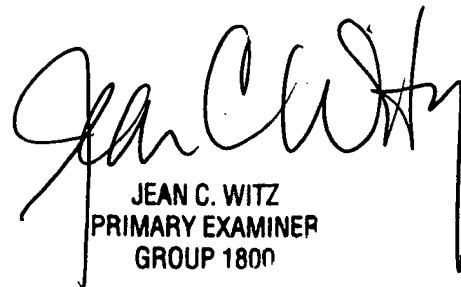
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5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073.

November 8, 1997

  
JEAN C. WITZ  
PRIMARY EXAMINER  
GROUP 1800